HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

# HPRA Safety Update

## COVID-19 Vaccines, Overview of National Reporting Experience
## Publication date: 09 December 2021 (Update #14)

### Highlights from this update:

- As of 30 November, a total of 16,313 reports of suspected side effects were notified to the HPRA. The number of COVID-19 vaccines administered as of that date was reported as 7,503,706. This includes 236,458 administered as a single dose, 3,624,114 as a first dose, 3,558,893 as a second dose and 84,241 as a third dose (for those with a weakened immune system).[1] Additionally, as of that date, 761,065 booster doses have been administered.[2]

- Whilst not experienced by everyone, all vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the benefits, given the risk of COVID-19 illness and related complications, and as scientific evidence shows that they reduce deaths and hospitalisations due to COVID-19. Overall, the national reporting experience continues to support the favourable assessment that the benefits of COVID-19 vaccines outweigh the risks. An overview of national reports received is provided in this safety update on page 5.

- On 03 December, the European Medicines Agency (EMA) published highlights from its monthly safety committee meeting, which included information on COVID-19 vaccines. On 09 December, the EMA published safety update reports for mRNA vaccines (Comirnaty®, Spikevax® [previously COVID-19 Vaccine Moderna®]) and adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®). These publications describe safety issues under evaluation, as well as any new recommendations. Topics of interest are summarised on page 7 of this update.

- The next HPRA safety update is due for publication on 20 January 2022.

[1] *Health Service Executive Vaccination Programme overview as of Tuesday 30 November 2021* *https://www.hse.ie/eng/services/news/newsfeatures/covid19-updates/vaccination-programme-dashboard-as-of-30-november-2021.pdf*

[2] *Government of Ireland GeoHive Vaccinations https://covid-19.geohive.ie/pages/vaccinations*

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## UNDERSTANDING THE DATA PRESENTED WITHIN THIS SAFETY UPDATE

This update includes an overview of reports of ***suspected side effects*** notified to the HPRA safety monitoring system and is provided as an enhanced transparency measure for members of the public and healthcare professionals. All vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the expected benefits in preventing COVID-19 illness.

Reports included in the overview are those notified to the HPRA on a voluntary basis by healthcare professionals and members of the public, with reporting of suspected side effects to COVID-19 vaccines (www.hpra.ie/report) encouraged. Any reports of Irish cases received by the HPRA from the company (i.e. the licence holder, to date, BioNTech, Moderna, AstraZeneca, Janssen) responsible for the vaccine are also included within this update. This overview provides an up-to-date summary of national reporting experience.

However, it is important to understand that conclusions on the safety of a vaccine cannot be drawn based on the information provided, given well-established and known limitations in interpreting such data in isolation, examples of which are described below.

### Causation

- The HPRA receives reports based on ***suspicion*** that an adverse experience may be associated with vaccination. This does not mean the vaccine ***caused*** the adverse experience**.** As such, these are referred to as ***'suspected'*** side effects.
- Reports may describe coincidental events, which have occurred post-vaccination, but would have occurred even if vaccination had not taken place (e.g. they may be due to an underlying medical condition, or be signs and symptoms of another illness).
- Each individual report is carefully reviewed, however, the totality of data from all sources (e.g. clinical and epidemiological studies and literature) must be considered as part of ongoing safety monitoring to ensure ***evidenced based conclusions*** are drawn.

### Number/volume

- As the HPRA system is based on voluntary reporting, ***not all*** suspected side effects will be reported. As such, the number and types of reports notified can vary for a variety of reasons.
- An increased number of reports is expected for COVID-19 vaccines, given public interest as well as HPRA calls encouraging reporting. This is known as ***stimulated reporting***.
- A single report may describe more than one suspected side effect in an individual (e.g. headache and nausea reported together), therefore, the number of side effects may exceed the total number of reports received.

### Comparisons

- The type and number of reports received for different COVID-19 vaccines are ***not directly comparable*** as, for example, the vaccines have not been used in the vaccination programme for the same length of time, and will have been administered to different numbers of people, with different underlying medical conditions and across different settings.

- Each vaccine is authorised on the basis that its benefits-risk profile has and continues to be favourable.

### Changes to data over time

- The description of suspected side effects in this update reflects available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as more data are reported and evaluated.
- For these reasons, the information in this report is not sufficient in isolation to draw conclusions on the safety profile of a vaccine. Like all vaccines, some side effects are to be expected, with the vast majority mild or moderte in intensity and resolving within a few days. Vaccines are approved for use on the basis of robust scientific evidence that demonstrates their benefits outweigh any risks.

***Always refer to the product information for information on the established safety profile, including known side effects of a COVID-19 vaccine.***

***This includes the Package Leaflet (for members of the public) and Summary of Product Characteristics (for healthcare professionals)***

Product information for COVID-19 vaccines is accessible here.

## AUTHORISED COVID-19 VACCINES

COVID-19 vaccines currently authorised for use in the European Union by the EMA include:

mRNA vaccines:

- Comirnaty® (licence holder: BioNTech Manufacturing GmbH) is authorised for use in individuals aged 5 years and older as a vaccination course consisting of two separate doses, with a third dose recommended for those who are severely immuncompromised. A booster dose may be administered at least 6 months after the second dose in individuals aged 18 years and older. For children aged 5 to 11 years of age, the dose of Comirnaty is lower than that used in people aged 12 and above (10 microgram compared with 30 microgram). For further information on this vaccine click here.
- Spikevax® (*previously COVID-19 Vaccine Moderna®)* (licence holder: Moderna Biotech Spain, S.L.) is authorised for use in individuals aged 12 years and older as a vaccination course consisting of two separate doses, with a third dose recommended for those who are severely immuncompromised. A booster dose may be administered at least 6 months after the second dose, in individuals aged 18 years and older. For further information on this vaccine click here.

Adenoviral vector vaccines:

- Vaxzevria® (licence holder: AstraZeneca AB) is authorised for use in individuals 18 years of age and older as a vaccination course consisting of two separate doses. For further information on this vaccine click here.
- COVID-19 Vaccine Janssen® (License holder: Janssen-Cilag International NV) is authorised for use in individuals aged 18 years and older as a single dose administration. For further information on the vaccine click here.

## OVERVIEW OF SUSPECTED SIDE EFFECT REPORTS

### Number of reports received

As of 30 November, the HPRA received 16,313 reports describing suspected side effects[3,4] in association with COVID-19 vaccines, as follows:

| | |
|---|---|
| mRNA vaccines (Comirnaty® and Spikevax®) | 9,983 |
| Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®) | 6,211 |
| Brand unknown/not specified | 119 |

Doses administered by vaccine type, as of 30 November, were reported as follows:[1]

- mRNA vaccines: 5,505,612 Comirnaty®, 570,708 Spikevax®.
- Adenoviral vector vaccines: 1,190,919 Vaxzevria®, 236,467 COVID-19 Vaccine Janssen®.

Further information on vaccination, including doses administered, is available from covid-19.geohive.ie.

### Regularly reported suspected side effects

The most regularly reported suspected side effects notified to the HPRA include the following:[5]

| mRNA vaccines (Comirnaty® and Spikevax®) |
|---|
| **10% or more of reports describe side effects such as:**<br>▪ Fever, pain (non-specific), tiredness<br>▪ Dizziness, headache<br>▪ Nausea<br><br>**1% to less than 10% of reports describe side effects such as:**<br>▪ Abdominal pain, diarrhoea, tingling sensation in mouth, vomiting<br>▪ Drowsy, fainting/feeling faint, migraine, numbness/reduced sensations, tingling/pins and needles/tremor<br>▪ Back pain, joint/limb pain, muscle pain/weakness/spasm/stiffness, neck pain<br>▪ Blurred vision<br>▪ Chest discomfort/pain, chills, general discomfort, feeling unwell, feeling hot/cold, flu-like symptoms, lack of energy/feeling weak, swelling including of legs/arms/face, underarm pain<br>▪ Cough, shortness of breath, sore throat<br>▪ Difficulty carrying out daily tasks (such as temporarily unable to attend work, need to stay in bed)<br>▪ Enlarged lymph nodes |

*[3]A single report may contain more than one suspected side effect for an individual (e.g. rash and hives reported together). Therefore, the total number of suspected side effects will exceed the total number of reports.*
*[4]In accordance with EU guidance, reports are valid if the minimum reporting criteria are met. These include an identifiable reporter, an identifiable patient, one or more suspected medicine known to have been administered and one or more suspected adverse reaction.*
*[5]Terms listed as frequently reported are presented according to standard coding classification system (MedDRA) adopted for use in the EU, and grouped by system organ class (SOC) and listed alphabetically. It should be noted that regular reporting of a side effect is not the same as the incidence of occurrence.*

- Feeling anxious, insomnia/trouble sleeping
- Increased heart rate/racing heart, increased blood pressure
- Injection site redness, pain, itchiness, swelling, rash, difficulty moving injected arm
- Lack of appetite
- Menstrual disturbances
- Skin reactions, skin red/red rash, sweating, general rash, itching, itchy rash, hives
- Tinnitus (ringing in the ears), vertigo-like symptoms

Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

**10% or more of reports describe side effects such as:**

- Chills, fever, tiredness
- Dizziness, headache
- Joint pain, muscle pain, other pain (non-specific)
- Nausea

**1% to less than 10% of reports received describe side effects such as:**

- Abdominal discomfort/pain, diarrhoea, vomiting
- Back pain, bone pain, limb pain, muscle spasms/weakness/stiffness, neck pain
- Chest discomfort/pain, general discomfort, feeling unwell/ill, feeling hot/cold, flu-like symptoms, lack of energy/weakness, swelling including of legs/arms
- Cough, shortness of breath, sore throat, nose bleed
- Difficulty carrying out daily tasks (such as temporarily unable to attend work, need to stay in bed)
- Drowsy, fainting, headache, migraine, numbness/reduced sensations, tingling/pins and needles, tremor
- Ear pain, tinnitus (ringing in the ears), vertigo-like symptoms
- Enlarged lymph nodes
- Eye pain, vision blurred
- Hives, skin red, general rash, sweating/cold sweat, itching, itchy rash
- Increased heart rate/racing heart
- Injection site pain, redness, swelling, bruising, difficulty moving injected arm
- Insomnia/trouble sleeping
- Lack of appetite
- Menstrual disturbances

The majority of regularly reported suspected side effects are consistent with the types of events typically observed following vaccination, including those described in the product information for the individual vaccines, and are mild to moderate in nature.

In reports evaluated, which include information on outcome, approximately 40% of suspected side effects had resolved or were resolving at the time of reporting. For others, the suspected side effects had not yet resolved, or the outcome was reported as unknown, when initially reported. Information on reports with a fatal outcome is provided on page 12.

A full breakdown of all suspected side effects described in reports is provided on page 13. Further information on how reports received by the HPRA are processed, including how safety signals are evaluated, is given on page 17.

The most recent EMA safety committee meeting highlights are available here.

## Topics of interest, including EMA recommendations

In this section, topics of interest, including any new recommendations from EMA's safety committee, are described. The information provided should be considered together with the approved product information which describes the established safety profile, including known side effects of a COVID-19 vaccine. This includes the Package Leaflet (for members of the public) and Summary of Product Characteristics (for healthcare professionals).

Product information for each authorised vaccine is available from the HPRA website here.

Topics of interest included in this safety update, are as follows:

### mRNA vaccines (Comirnaty® and Spikevax®)

- Booster or third dose
- Vaccination of adolescents (12 to 17 years)
- Myocarditis and pericarditis

### Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

- Cutaneous small vessel vasculitis and COVID-19 Vaccine Janssen®
- Thrombosis with thrombocytopenia syndrome (TTS) and cerebral venous sinus thrombosis (CVST)
- Transverse myelitis and COVID-19 Vaccine Janssen®

### Common topics

- Allergic type reactions (also known as hypersensitivity)
- Menstrual disturbances
- Deaths following vaccination

## mRNA vaccines (Comirnaty® and Spikevax®)

#### Reports following a booster or third dose

- As the national vaccination programme continues, the HPRA are closely monitoring reports of suspected side effects received following a third dose (for people with a weakened immune system) or a booster dose.
- As of 30 November, the HPRA received 100 reports of suspected side effects following either a third or booster dose of Comirnaty® or Spikevax®. As of that date, 84,241 third doses[1] and 761,065 booster doses[2] had been administered as part of the national vaccination program.
- Overall, the reports received are consistent with the types of reports received after the primary vaccination course with the majority mild to moderate in nature. The most regularly reported include fever, headache, tiredness, nausea and chills.

### Vaccination of adolescents (12 to 17 years)

- As the national vaccination programme continues, the HPRA are closely monitoring any reports of suspected side effects received in adolescents aged 12 to 17 years.
- As of 30 November, the HPRA has received 222 reports of suspected side effects following vaccination of an adolescent with an mRNA vaccine. A breakdown of all suspected side effects by type, reported in those aged 12 to 17 years is available on page 16.
- Overall, the reports received are consistent with the types of reports received for adults, with most being mild to moderate in nature. Of the reports received which include information on outcome, many of the suspected side effects had resolved or were resolving at the time of reporting.

### Reports of myocarditis and pericarditis

- Myocarditis and pericarditis are inflammatory conditions of the heart and are very rare side effects of Comirnaty® and Spikevax®. Myocarditis and pericarditis can also occur for other reasons, such as due to an immune disorder or following a viral infection, such as COVID-19.
- The EMA's safety committee reviewed recent data on the known risk of myocarditis/pericarditis following vaccination, including from two large studies that took place in France (Epi-phare) and the Nordic countries (Sweden, Finland, Denmark, Norway). Overall, the outcome of the review confirms information already known about the risk for these mRNA vaccines, and provides some further details on these two conditions, including on frequency (how often this event occurs).
- Based on the reviewed data, it has been determined that the risk for both of these conditions is overall "very rare", meaning that up to one in 10,000 vaccinated people may be affected.
- Additionally, the data show that the increased risk of myocarditis after vaccination is highest in younger males. The French and Nordic studies provide estimates of the number of cases of myocarditis in vaccinated younger males following the second dose, compared to unvaccinated persons of the same age and gender (i.e. background events), as follows:
  - For Comirnaty®, the French study showed that in a period of seven days after the second dose, there were about 0.26 extra cases of myocarditis in 12 to 29 year old males per 10,000 compared to unvaccinated persons. In the Nordic study, in a period of 28 days after the second dose there were 0.57 extra cases of myocarditis in 16 to 24 year-old males per 10,000, compared to unvaccinated persons.
  - For Spikevax®, the French study showed that in a period of seven days after the second dose there were about 1.3 extra cases of myocarditis in 12 to 29 year old males per 10,000 compared to unvaccinated persons. In the Nordic study, in a period of 28 days after the second dose there were around 1.9 extra cases of myocarditis in 16 to 24 year old males per 10,000 compared to unvaccinated persons.
- The EMA also confirmed following this review that the benefits of these vaccines continue to outweigh their risks, given the risk of COVID-19 illness and related complications, and as scientific evidence shows that they reduce deaths and hospitalisations due to COVID-19. Further information on the review is available here.

- Current advice is that whilst the risk of myocarditis and pericarditis following vaccination is very rare, those vaccinated (or their parents/caregivers) are advised to seek immediate medical attention if symptoms indicative of myocarditis or pericarditis occur. The symptoms can vary but may include chest pain, breathlessness and/or a forceful heartbeat that may be irregular (palpitations). Myocarditis and pericarditis can develop within just a few days after vaccination, with the majority of cases occuring within 14 days and more often after the second vaccination as compared to the first. The risk after a third or booster dose is being carefully monitored. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.
- For Comirnaty® and Spikevax®, as of 30 November, the HPRA received a total of 92 reports describing suspected side effects of myocarditis (32 reports), pericarditis (39 reports) or a combination of both (21 reports). Of these, 81 occurred following vaccination with Comirnaty® and 11 following Spikevax®. In relation to dose, 40 cases occurred after the first dose, 48 after the second dose and a small number[6] for which the information was not reported. Most occurred within 14 days of vaccination. Suspected cases were reported in 64 males and 28 females, with a median age of 36 years (range 12 to 81). In five cases, the report concerned an adolescent ( i.e. aged 12 to 17 years).
- National reports received describe symptoms such as chest pain/discomfort, palpitations, dizziness, irregular heartbeat and shortness of breath. In a number of cases, possible alternative explanations (other than vaccination) for the individual developing the condition were described, or the diagnosis was provisional and not yet finalised at the time of reporting. In the majority of the cases, the individuals were still recovering or had ongoing symptoms at the time of initial reporting.
- All reports of myocarditis and pericarditis notified to the HPRA are carefully reviewed. However, it can be expected that medical events due to various causes will continue to occur, including following vaccination, but which are not all necessarily caused by the vaccine.

## Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

### Reports of cutaneous small vessel vasculitis (CSVV) with COVID-19 Vaccine Janssen®.

- Cutaneous small vessel vasculitis (CSVV) is a skin disorder which involves inflammation of the skin's blood vessels, which can cause a rash, red or purple spots under the skins surface, or bruising. It can occur due to an underlying infection or as a response to medicines or vaccines, and usually resolves by itself.
- The EMA's safety committee has recommended that product information for COVID-19 Vaccine Janssen® be updated to include CSVV as a possible side effect, following a review of a small number[6] of reports. While the exact frequency (how often this event occurs) following

[6] *When the relevant number is less than five, it is described as a small number to avoid any potential, inadvertent identification of the individuals concerned.*

vaccination is unknown, the recommendation follows a review of 37 cases reported worldwide from an estimated 36 million doses administered.

- To date, no reports of CSVV following COVID-19 Vaccine Janssen® have been notified to the HPRA.
- Further information is available from the EMA safety update report for COVID-19 Vaccine Janssen®.

**Reports of thrombosis with thrombocytopenia syndrome (TTS) and cerebral venous sinus thrombosis (CVST)**

- Thrombosis with thrombocytopenia syndrome (TTS) is a very rare side effect associated with Vaxzevria® and COVID-19 Vaccine Janssen®. The syndrome involves an unusual combination of thrombosis (blood clots) together with thrombocytopenia (very low platelet levels).
- Vaccine recipients are reminded to seek immediate medical attention if they experience any of the following signs and symptoms: shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain post vaccination, severe or persistent headaches, blurred vision, confusion, seizures (fits) or bruising beyond the site of vaccination after a few days.
- Healthcare professionals are reminded that individuals diagnosed with thrombocytopenia within three weeks after vaccination should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. Healthcare professionals should be alert to the signs and symptoms of TTS and consult applicable guidance and/or appropriate specialists to diagnose and treat this condition. A second dose of Vaxzevria® is contraindicated in any person who experienced TTS following their first dose. Advice to healthcare professionals previously issued on this topic is available from the HPRA website here.
- As of 30 November, the HPRA has received 10 reports that are suspected cases of TTS, and which mostly describe the unusual combination of blood clotting in combination with low platelets. In relation to these suspected TTS cases, symptoms occurred between 1-5 weeks of vaccination with a first dose of Vaxzevria® or single dose of COVID-19 Vaccine Janssen®. The types of symptoms reported include shortness of breath, severe and/or persistent headache, unusual skin bruising, abdominal pain, leg pain and leg swelling. Cases occurred in both males and females, with a median age of 36 (age range, 21 to 63 years). In a small number, blood clots occurred in unusual locations, including in the brain (cerebral venous sinus thrombosis, CVST) and liver (hepatic and portal veins). Based on information currently available, the individuals are either discharged or recovering in hospital after receiving specialist medical care.
- The EMA's safety committee also recently reviewed a very small number of cases of CVST, reported without low platelets, and mainly within four weeks of vaccination with Vaxzevria®. Product information will be updated to highlight that these cases have occurred very rarely after vaccination, and that healthcare professionals should consider this in particular for those at higher risk of CVST. These events are distinct from CVST reported as part of TTS and may require a different approach to treatment. Further information on this review is available here. The HPRA

has received a small number[6] of reports of CVST without low platelets following vaccination with Vaxzevria®, and for which the outcome was reported as recovered.

### Reports of transverse myelitis and COVID-19 Vaccine Janssen®

- Transverse myelitis is a rare disorder caused by inflammation to the spinal cord, which interrupts communication between nerve cells in the spinal cord and the rest of the body, and can result in altered sensations, bladder and bowel dysfunction, pain and weakness. The underlying cause is often unknown but may be related to an immune system disorder or an infection.
- Transverse myelitis has been reported very rarely following vaccination with COVID-19 Vaccine Janssen® and the EMA's safety committee previously recommended that product information be updated to include transverse myelitis as a potential side effect.
- As of 30 November, the HPRA has received a small number[6] of reports of transverse myelitis following vaccination with COVID-19 Vaccine Janssen®. The exact frequency (how often this event occurs) following vaccination is as of yet unknown.

## COVID-19 vaccines - Common topics

### Reports of allergic type reactions (also known as hypersensitivity)

- Allergic type reactions are known side effects of both mRNA and adenoviral vector vaccines. The HPRA has received a number of such reports, mainly describing symptoms such as itchiness, hives and rash. In some cases, medical treatment and/or clinical observation of the individual was needed.
- The HPRA continues to monitor reports of anaphylaxis, which is a serious allergic reaction. All reports suggestive of anaphylaxis (e.g. sudden onset of symptoms such as low blood pressure, collapse, rapid heart rate, shortness of breath, swelling of lips/throat and itchy skin) are carefully reviewed. Cases are classified by the HPRA as anaphylaxis using a well-established set of clinical and laboratory criteria however, some reports do not contain sufficient detail for classification purposes.[7] Of the cases reviewed, 12 reports following an mRNA vaccine and a small number[6] of reports following an adenoviral vector vaccine are currently classified as anaphylaxis. In some cases the individual concerned had recovered at the time of reporting and the remaining cases are being followed-up for further information.
- Anaphylaxis is a known side effect, and information on managing this risk is described in the product information. As for all vaccines, COVID-19 vaccines should be administered under close supervision with appropriate medical treatment available in case of such a reaction. Those vaccinated should discuss any signs/symptoms of allergic reaction that they are concerned about with a healthcare professional.

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*[7]Reports classified using Brighton Collaboration case definition for anaphylaxis https://brightoncollaboration.us/category/pubstools/case-definitions/. Some reports contain limited information and therefore it is not possible to classify according to the Brighton Collaboration case definition. In these case, the HPRA follows up with the reporter for the missing information.*

### Reports of menstrual disturbances

- Menstrual disturbances are one of the more regularly reported side effects to the HPRA (see pages 5 & 6). In the vast majority of caes, reports are received directly from a vaccinated woman, and describe a recent disturbance in normal menstruation, such as a period arriving earlier or later than expected, or of a heavier nature than normal. Whilst less frequent, some reports that describe a bleeding event in a woman who is post menopausal have also been notified.
- Following evaluation of the available data in relation to menstrual disorders, the EMA's safety committee concluded that no specific pattern of menstrual disturbances could be found and there is currently no evidence suggesting a causal association or link between menstrual disturbances and vaccination with any of the authorised COVID-19 vaccines. Further details on the safety reviews are available here: Comirnaty®, Spikevax®, Vaxzevria® and COVID-19 Vaccine Janssen®.
- The EMA has highlighted that generally, menstrual disturbances are very common and can occur with or without an underlying medical condition. In about half of the cases reviewed, the patient's medical history or other medication being used provided a possible explanation for their symptom. The EMA outlined that menstrual disturbances may occur due to a wide range of reasons, including stress or tiredness and conditions such as fibroids and endometriosis. Women who are concerned about prolonged or severe menstrual disturbances may wish to seek medical advice, in particular if unexpected vaginal bleeding, for example, in a postmenopausal women, is experienced.

### Reports of deaths following COVID-19 vaccination

- A total of 94 reports have been received describing an individual who was known to have been vaccinated and subsequently passed away. Of these, 83 were reported with an mRNA vaccine, seven with adenoviral vector vaccines and the remaining four were reported with brand unknown/not specified. The majority of reports (approximately 80%) with a fatal outcome describe an individual aged 75 years and over, with the median age of the individuals being 83 years. Of those, 49 deaths occurred in males and 44 in females, with the sex not provided in one report. For a number of reports, the cause of death was unconfirmed at the time of reporting, with post mortem results awaited.
- Reports describing a death are carefully reviewed. However, it can be expected that fatalities due to progression of underlying disease or natural causes will continue to occur, including following vaccination. This does not mean that the vaccine caused the deaths.

## BREAKDOWN OF SUSPECTED SIDE EFFECTS BY CATEGORY

A full breakdown of all suspected side effects described in reports received by the HPRA is provided below by vaccine type (i.e. mRNA and adenoviral vector vaccines) and by category (i.e. the related body system). Whilst the vast majority of reports notified to the HPRA describe expected events (i.e. known side effects of a vaccine or vaccination process), reports can also be received for events that are unexpected and/or are considered serious, as they required medical care or intervention. Such reports may describe events not caused by the vaccine and may have occurred coincidentally. However, all reports are carefully reviewed and if there is cause to do so, a further analysis is carried out to determine if a vaccine may have had a contributory role. If it is determined that a vaccine is a contributory factor, the public and healthcare professionals will be informed and the relevant product information will be updated.

**Please read the following explanatory note in relation to understanding the data presented in the suspected side effect tables:**

- A single report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, which may include more than one category, or more than one in a specific category. For example, a single report that describes chills, fatigue and nausea in an individual, includes three suspected side effects, two in general symptoms (chills and fatigue) and one in gastrointestinal (nausea). As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.
- The breakdown summary includes all suspected side effects as they are reported to the HPRA. This includes cases for which a diagnosis is reported as provisional, or for which there is more than one possible diagnosis at the time of reporting. In other cases, a diagnosis may not be available, and only signs and symptoms or laboratory test results are given. Reports are also received from members of the public, and the HPRA follows up to medically confirm these reports, where consent is provided and more information is required. For each report, all events are 'coded'[8] as suspected side effects in the national pharmacovigilance database using the exact information (verbatim) given in the report. The HPRA follows up with the reporter to collect any further information which may be relevant to the assessment of the case.
- The description of suspected side effects in this update, including the number and category, reflect available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as reports are further evaluated.
- Please refer to the section 'Understanding the data presented within this safety update' on page 3 with regard to further interpretation guidance. Background information on the evaluation of suspected side effect reports is available on page 17.

Of the 16,313 reports notified to the HPRA as of 30 November, over 75% have now been submitted to EMA's Eudravigilance database, and as such, additional anonymised information on these reports, is publicly available through the following link www.adrreports.eu. See page 17 for further details.

[8] *Medical Dictionary for Regulatory Activities (MedDRA) https://www.meddra.org/*

### Suspected side effects to mRNA vaccines

A breakdown of suspected side effects described in the 9,983 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

| Category | Suspected side effects |
|---|---|
| General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling* | 11,646 |
| Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint* | 6,668 |
| Muscles, tissue, bones or joints *e.g. general muscular pain or weakness* | 4,579 |
| Gastrointestinal *e.g. nausea, vomiting, diarrhoea* | 3,315 |
| Skin *e.g. rash, itchy rash* | 2,621 |
| Reproductive system, obstetrics or gynaecology related *e.g. menstrual disturbance* | 1,602 |
| Respiratory *e.g. cough, shortness of breath* | 1,399 |
| Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping* | 1,100 |
| Social circumstances *e.g. need to rest in bed or take a break from normal daily activities* | 861 |
| Cardiac (heart) related *e.g. palpitations* | 838 |
| Eye *e.g. eye pain, vision blurred* | 745 |
| Blood and lymphatic system *e.g. swollen glands* | 734 |
| Procedural issues and complications *e.g. injection site bruising* | 641 |
| Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)* | 612 |
| Infection *e.g. local or general such as influenza or cold sore* | 523 |
| Blood vessel related (i.e. veins/arteries) *e.g. pale complexion* | 511 |
| Ear related e*.g. earache, tinnitus* | 460 |
| Metabolism and nutrition disorders *e.g. decreased appetite* | 303 |
| Immune system related *e.g. hypersensitivity, allergic reaction* | 152 |
| Kidney related *e.g. change in frequency of urination* | 91 |
| Endocrine (hormone) *e.g. thyroid function change* | 23 |
| Liver related *e.g. jaundice, inflammation* | 22 |
| Cysts and polyps *e.g. benign skin growth* | 11 |

### Suspected side effects to adenoviral vector vaccines

A breakdown of suspected side effects described in the 6,211 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

| Category | Suspected side effects |
|---|---|
| General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling* | 10,725 |
| Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint* | 5,598 |
| Muscles, tissue, bones or joints *e.g. general muscular pain or weakness* | 3,909 |
| Gastrointestinal *e.g. nausea, vomiting, diarrhoea* | 2,957 |
| Skin *e.g. rash, itchy rash* | 1,657 |
| Respiratory *e.g. cough, shortness of breath* | 902 |
| Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping* | 801 |
| Social circumstances *e.g. need to rest in bed or take a break from normal daily activities* | 652 |
| Eye *e.g. eye pain, vision blurred* | 479 |
| Reproductive system, obstetrics or gynaecology related e.g. *menstruation disturbance* | 481 |
| Metabolism and nutrition disorders *e.g. decreased appetite* | 466 |
| Blood vessel related (i.e. veins/arteries) *e.g. pale complexion* | 438 |
| Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)* | 402 |
| Cardiac (heart) related *e.g. palpitations* | 371 |
| Procedural issue or complications *e.g. injection site bruising* | 356 |
| Ear related e*.g. earache, tinnitus* | 355 |
| Infection *e.g. local or general such as influenza or cold sore* | 253 |
| Blood and lymphatic system *e.g. swollen glands* | 182 |
| Kidney related *e.g. increased frequency of urination* | 70 |
| Immune system related *e.g. hypersensitivity, allergic reactions* | 58 |
| Liver related *e.g. jaundice* | 11 |
| Endocrine (hormone) *e.g. thyroid function change* | 10 |
| Cysts and polyps | <5 |

**Suspected side effects in adolescents (aged 12 to 17 years) following vaccination with an mRNA Vaccine**

A breakdown of suspected side effects described in the 222 reports notified to the HPRA concerning adolescents aged 12 to 17 years following vaccination with an mRNA vaccine is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

| Category | Suspected side effects |
|---|---|
| General symptoms and local reactions *e.g. tiredness, weakness, chest pain, feeling hot* | 211 |
| Nervous system *e.g. dizziness, headache, fainting or feeling faint* | 161 |
| Gastrointestinal *e.g. nausea, vomiting, abdominal pain* | 102 |
| Muscles, tissue, bones or joints *e.g. limb, muscle, joint pain* | 64 |
| Skin *e.g. rash, sweating* | 62 |
| Respiratory *e.g. shortness of breath, nose bleed* | 53 |
| Cardiac (heart) related *e.g. palpitations/racing heart* | 30 |
| Behavioural, emotional and mental health *e.g. trouble sleeping* | 27 |
| Social circumstances *e.g. need to rest in bed or take a break from normal daily activities* | 25 |
| Reproductive system, obstetrics or gynaecology related *e.g. menstruation disturbance* | 22 |
| Eye *e.g. vision blurred* | 20 |
| Blood vessel related (i.e. veins/arteries) *e.g. pale complexion* | 17 |
| Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. changes in heart rate* | 16 |
| Blood and lymphatic system *e.g. swollen glands* | 14 |
| Infection *e.g. chest infection* | 14 |
| Ear related *e.g. earache, tinnitus* | 12 |
| Procedural issue or complications *e.g. fall* | 12 |
| Metabolism and nutrition disorders *e.g. decreased appetite* | 10 |
| Immune system related | <5 |
| Kidney related | <5 |

## BACKGROUND INFORMATION ON THE EVALUATION OF SUSPECTED SIDE EFFECT REPORTS

As for all medicines and vaccines, suspected side effect reports in association with COVID-19 vaccines submitted to the HPRA are recorded and stored on the HPRA's national adverse reactions database. They are subsequently submitted (with any personal identifiers and contact details removed) to the EudraVigilance database operated and managed by the European Medicines Agency (EMA). EudraVigilance provides for the transfer of reports from national regulatory agencies such as the HPRA and marketing authorisation holders to the EMA. This supports early detection and monitoring of possible safety signals in relation to reported side effects.

The EMA also make available anonymised information on all reports, based on global safety experience, publically available through the following link www.adrreports.eu. The EMA also publish regular safety updates for COVID-19 vaccines, as well as highlights from meetings of the EMA's safety committee (Pharmacovigilance Risk Assessment Committee), which describe safety issues under review, as well as recommendations to revise product information. These are available via www.ema.europa.eu.

Information from side effect reports, together with additional safety data (e.g. from the scientific literature, cumulative safety data analysis, epidemiological studies etc.) are assessed on an on-going basis, in conjunction with our EU counterparts to consider their impact on the known safety profile of the COVID-19 vaccines and any need for regulatory changes to support safe and appropriate use.

Partially anonymised details of reports are also shared with other bodies also involved in safety monitoring of medicines, in accordance with the legislative provisions, including GDPR (please see the HPRA privacy statement here). These bodies include the World Health Organisation (WHO) and as appropriate, the company(ies) that hold the licence(s) for the medicine(s) concerned (i.e. marketing authorisation holders or 'MAHs'). Sharing of this information ensures that the information is available to all parties responsible for the ongoing safety monitoring of medicines.

Further information to support interpretation of the data provided in this update is available here.